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British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017

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TB, ADB, LCC, MC, TH, EM, RM, CN-P, CMO, RP, EPe, EPo, EJS, JS, CSt, VV and RBW contributed equally to this project and are listed alphabetically.

The multi-disciplinary guideline development group (GDG) comprised medical specialists (consultants in dermatology, paediatric dermatology, rheumatology, virology and obstetric medicine), a clinical nurse specialist, dermatology trainees, two patient representatives and a research team providing technical and methodological support.

Produced in 2005 by the British Association of Dermatologists

Reviewed and updated in 2009, 2017

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Key words: biologic therapy, psoriasis, guideline, systematic review, meta-analysis, network meta-analysis, GRADE



NICE has renewed accreditation of the process used by the British Association of Dermatologists to produce clinical guidelines. The renewed accreditation is valid until 31 May 2021 and applies to guidance produced using the processes described in Updated guidance for writing a British Association of Dermatologists clinical guideline – the adoption of the GRADE methodology 2016. The original accreditation term began on 12 May 2010. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

PURPOSE AND SCOPE OF THE GUIDELINE

The overall aim of the guideline is to provide evidence-based recommendations on the use of biologic therapies (adalimumab, etanercept, infliximab, ixekizumab, secukinumab and ustekinumab) in adults, children and young people for the treatment of psoriasis; consideration is given to the specific needs of people with psoriasis and psoriatic arthritis. Biologic therapies have now been in use for over 10 years, and with accrued patient-years exposure and clinical experience, many areas that were covered in previous versions of the guideline are now part of the Summary of Product Characteristics (SPC) and/or routine care so that specific recommendations are redundant (see Toolkit A: Summary of licensed indications and posology for biologic therapy, in *Supporting information 2*). Therefore, in this update we focus on areas where there has been a major change in the evidence base or clinical practice, where practice is very varied and/or where clear consensus or guidelines are lacking (see section 3.1 in *Supporting information 1*).

This set of guidelines has been developed using the BAD's recommended methodology¹ with reference to the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument [www.agreetrust.org]² and the Grading of Recommendations Assessment, Development and Evaluation (GRADE).³ Recommendations were developed for implementation in the NHS (U.K.). Note that the guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline assumes that prescribers cross-reference a drug's SPC to inform clinical decision-making for individual patients. Where relevant, this guidance applies to biosimilars (similar biological medical products), subject to recommendations given within the BAD position statement⁴ and EMA guidelines.⁵ This guidance does not cover agents licensed outside the UK or use of biologic therapies for indications other than psoriasis or use when psoriatic arthritis is the main indication.

To aid implementation, this executive summary contains only key clinical findings and recommendations (see Table 2) derived from systematic review of the evidence. The strength of recommendation is expressed by the wording and symbols featured in Table 1. Good practice point (GPP) recommendations are derived from informal consensus. A decision aid, informed by the evidence reviews, has been developed to help patients and clinicians choose the appropriate biologic therapy (see Table 3) and a suggested schedule for screening and monitoring (see Table 4) is also provided. The full version of the guideline is available online (*Supporting information 1*) and includes details on methodology, six systematic reviews with appraisal and discussion of the clinical evidence.

Strength	Wording	Symbols	Definition
Strong recommendation <i>for</i> the use of an intervention	"Offer" (or similar, e.g. "Provide", "Advise", "Screen", etc.)	↑↑	Benefits of the intervention outweigh the risks; most patients would choose the intervention whilst only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policy makers, it would be a useful performance indicator.
Weak recommendation <i>for</i> the use of an intervention	"Consider"	↑	Risks and benefits of the intervention are finely balanced; many patients would choose the intervention but many would not; clinicians would need to consider the pros and cons for the patient in the context of the evidence; for policy makers, it would be a poor performance indicator where variability in practice is expected.
No recommendation		⊖	Insufficient evidence to support any recommendation.
Strong recommendation <i>against</i> the use of an intervention	"Do not offer"	↓↓	Risks of the intervention outweigh the benefits; most patients would <i>not</i> choose the intervention whilst only a small proportion would; for clinicians, most of their patients would <i>not</i> receive the intervention.

Table 1. Strength of recommendation ratings

SUMMARY OF RECOMMENDATIONS

The evidence- and consensus-based (GPP) recommendations listed in Table 2 below should be implemented in the context of the evidence and discussions in the full version of the guideline.

Recommendations		Strength
Using biologic therapy		
R1	Initiation and supervision of biologic therapy for people with psoriasis should be undertaken by specialist physicians experienced in the diagnosis and treatment of psoriasis. Routine monitoring may be delegated to other healthcare professionals, for example, clinical nurse specialists. Manage psoriatic arthritis and/or multi-morbidity in consultation with the relevant healthcare professionals.	↑↑
R2	Agree and formalise arrangements for drug administration, monitoring and follow-up between health carers and the person receiving treatment	↑↑
R3	Offer people with psoriasis who are starting biologic therapy the opportunity to participate in long-term safety registries (in the U.K. and Republic of Ireland the British Association of Dermatologists Biologic Interventions Register, BADBIR ¹)	↑↑
Criteria for biologic therapy		
R4	Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated ¹¹ and the psoriasis has a large impact on physical, psychological or social functioning (for example, a DLQI or cDLQI of >10 or clinically relevant depressive or anxiety symptoms) and one or more of	↑↑

¹ <http://www.badbir.org/>

¹¹ Please see NICE guidelines CG153 for more information on contraindications and reviewing treatment response to phototherapy and systemic therapy

	<p>the following disease severity criteria apply:</p> <ul style="list-style-type: none"> the psoriasis is extensive (defined as BSA >10%, or a PASI ≥10, or at least 'moderate' on physician's global assessment^{III}) the psoriasis is severe at localised sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of high-impact and difficult-to-treat sites such as the face, scalp, palms, soles, flexures and genitals) 	
R5	Consider biologic therapy earlier in the treatment pathway (for example, if methotrexate has failed, is not tolerated or is contra-indicated) in people with psoriasis that fulfils the disease severity criteria and who also have active psoriatic arthritis ^{IV} or who have psoriasis that is persistent (i.e. that relapses rapidly off a therapy that cannot be continued long-term ^V)	↑
Prescribing biologic therapy		
R6	Be aware of the benefits of, contraindications to and adverse effects associated with biologic therapies and reference the drug-specific SPCs ^{VI}	↑↑
R7	Provide high-quality, evidence-based information to people being prescribed biologic therapies. Explain the risks and benefits to people undergoing this treatment (and their families or carers where appropriate), using absolute risks and natural frequencies when possible (see Table 3: Decision aid). Allow them adequate time to consider the information.	↑↑
R8	Support and advice should be offered to people with psoriasis (and their families or carers where appropriate) by healthcare professionals who are trained and competent in the use of biologic therapies	↑↑
Reviewing biologic therapy		
R9	Assess initial response to biologic therapy in people with psoriasis at time points appropriate for the drug in question, and then on a regular basis during therapy (for example, every 6 months)	↑↑
R10	<p>Review response to biologic therapy by taking into account:</p> <ul style="list-style-type: none"> psoriasis disease severity compared with baseline (for example, Psoriasis Area and Severity Index [PASI] baseline to endpoint score^{VII}) the agreed treatment goal control of psoriatic arthritis disease activity and/or inflammatory bowel disease (in consultation with a rheumatologist and/or gastroenterologist) the impact of psoriasis on the person's physical, psychological and social functioning the benefits versus the risks of continued treatment the views of the person undergoing treatment (and their family or carers, where appropriate) adherence to the treatment 	↑↑

^{III} Physician's global assessment clear, nearly clear, mild, moderate, severe, very severe

^{IV} Please see <http://pathways.nice.org.uk/pathways/musculoskeletal-conditions#content=view-node%3Anodes-psoriatic-arthritis&path=view%3A/pathways/musculoskeletal-conditions/arthritis.xml>

^V Rapid relapse is defined as greater than 50% of baseline disease severity within 3 months of completion of any treatment (for example narrow band UVB)

^{VI} www.medicines.org.uk/emc/

^{VII} <http://www.bad.org.uk/healthcare-professionals/forms-downloads>

R11	Assess whether the minimal response criteria have been met, as defined by: <ul style="list-style-type: none">a 50% or greater reduction in baseline disease severity (for example, PASI 50 response, or % BSA where the PASI is not applicable) andclinically relevant improvement in physical, psychological or social functioning (for example, a 4-point or greater improvement in DLQI or resolution of low mood)	↑													
R12	Consider changing to an alternative therapy, including another biologic therapy, if any of the following applies: <ul style="list-style-type: none">the psoriasis does not achieve the minimum response criteria (primary failure – see R11)the psoriasis initially responds but subsequently loses this response (secondary failure)the current biologic therapy cannot be tolerated or becomes contraindicated	↑													
Choice of biologic therapy: general considerations															
R13	Take into account both psoriasis and psoriatic arthritis before initiating or making changes to biologic therapy, and: <ul style="list-style-type: none">manage treatment in consultation with a rheumatologist or paediatric rheumatologistbe aware that the presence of and phenotype of psoriatic arthritis (for example, peripheral versus axial disease) may influence access to, choice and dose of, biologic therapy	↑↑													
R14	Tailor the choice of agent to the needs of the person and take into account the following factors (see Table 3: Decision aid): <table><tr><td>Psoriasis factors</td></tr><tr><td>the goal of therapy (for example a PGA of clear or nearly clear)</td></tr><tr><td>disease phenotype and pattern of activity</td></tr><tr><td>disease severity and impact</td></tr><tr><td>the presence of psoriatic arthritis (in consultation with an adult or paediatric rheumatologist)</td></tr><tr><td>outcomes to previous treatments for psoriasis</td></tr><tr><td>Other factors</td></tr><tr><td>person's age</td></tr><tr><td>past or current co-morbid conditions (for example, inflammatory bowel disease, cardiovascular disease)</td></tr><tr><td>conception plans</td></tr><tr><td>body weight</td></tr><tr><td>the person's views and any stated preference on administration route or frequency</td></tr><tr><td>adherence</td></tr></table>	Psoriasis factors	the goal of therapy (for example a PGA of clear or nearly clear)	disease phenotype and pattern of activity	disease severity and impact	the presence of psoriatic arthritis (in consultation with an adult or paediatric rheumatologist)	outcomes to previous treatments for psoriasis	Other factors	person's age	past or current co-morbid conditions (for example, inflammatory bowel disease, cardiovascular disease)	conception plans	body weight	the person's views and any stated preference on administration route or frequency	adherence	↑↑
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adherence															
R15	Be aware that the recommended first-line choice of biologic therapy will not be appropriate for every individual; use the decision aid and with reference to R14 to inform choice of alternative licensed biologic therapies.	↑↑													
Choice of biologic therapy in adults: first line															
R16	Offer ustekinumab as a first-line biologic agent to adults with psoriasis who fulfil the criteria for biologic therapy (see also R4 and R5)	↑↑													

R17	Offer adalimumab as a first-line biologic agent to adults with psoriasis particularly when psoriatic arthropathy is a consideration	↑↑												
R18	Consider secukinumab as a first-line biologic agent in adults with psoriasis, with or without psoriatic arthritis	↑												
Choice of biologic therapy in adults: second line														
R19	Offer any of the currently licensed biologic therapies when psoriasis has not responded to a first biologic therapy. Use the decision aid (Table 3) and take into account all factors detailed in R14 to select the most appropriate agent.	↑↑												
Consideration														
R20	Reserve infliximab for use in people with very severe disease ^{viii} or where other available biologic agents have failed or cannot be used	↑↑												
What to do when a second or subsequent biologic therapy fails in adults														
R21	<p>When a person’s psoriasis responds inadequately to a second or subsequent biologic agent seek advice from a clinician with expertise in biologic therapy and consider any of the following strategies:</p> <ul style="list-style-type: none">reiterate advice about modifiable factors contributing to poor response (for example, obesity and poor adherence)optimise adjunctive therapy (for example, switch from oral to sub-cutaneous methotrexate)switch to an alternative biologic agentconsider non-biologic therapy approaches (for example inpatient topical therapy, phototherapy or standard systemic therapy)	↑												
When to consider dose escalation														
R22	<p>Consider escalating the dose of biologic therapy in adults, where this is feasible and funded (see table below) when an inadequate primary response may be due to insufficient drug dosing (for example, in people who are obese or whose psoriasis relapses during the treatment cycle). Take into account that this may be associated with an increased risk of infection, and, depending on the drug, off-licence.</p> <table><tr><th>Biologic agent</th><th>Suggested dose-escalation strategy</th></tr><tr><td>Ustekinumab 45 mg every 12 weeks (<100 kg)</td><td>Ustekinumab 90 mg every 12 weeks (<100 kg)^{ix}</td></tr><tr><td>Ustekinumab 90 mg every 12 weeks (>100 kg)</td><td>Ustekinumab 90 mg every 8 weeks (>100 kg)^{ix}</td></tr><tr><td>Adalimumab 40 mg every other week</td><td>Adalimumab 40 mg weekly</td></tr><tr><td>Etanercept 50 mg once weekly</td><td>Etanercept 50 mg twice weekly</td></tr><tr><td>Infliximab 5 mg/kg every 8 weeks</td><td>Infliximab 5 mg/kg every 6 weeks^{ix}</td></tr></table>	Biologic agent	Suggested dose-escalation strategy	Ustekinumab 45 mg every 12 weeks (<100 kg)	Ustekinumab 90 mg every 12 weeks (<100 kg) ^{ix}	Ustekinumab 90 mg every 12 weeks (>100 kg)	Ustekinumab 90 mg every 8 weeks (>100 kg) ^{ix}	Adalimumab 40 mg every other week	Adalimumab 40 mg weekly	Etanercept 50 mg once weekly	Etanercept 50 mg twice weekly	Infliximab 5 mg/kg every 8 weeks	Infliximab 5 mg/kg every 6 weeks ^{ix}	↑
Biologic agent	Suggested dose-escalation strategy													
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Etanercept 50 mg once weekly	Etanercept 50 mg twice weekly													
Infliximab 5 mg/kg every 8 weeks	Infliximab 5 mg/kg every 6 weeks ^{ix}													
Choice of biologic therapy in children and young people														
R23	Offer adalimumab (≥ 4 years), etanercept (≥ 6 years) or ustekinumab (≥ 12 years) to children and young people who fulfil the criteria for biologic therapy (see also R4 and R5)	↑↑												
R24	When a child’s or young person’s psoriasis responds inadequately to a first or subsequent	↑												

^{VIII} 'Very severe' relates to the physician's global assessment or/and the NICE definition ((PASI 20 or more and DLQI 18 or more) and failed to respond to standard systemic therapies such as ciclosporin, methotrexate or PUVA (psoralen and long-wave ultraviolet radiation), or the person is intolerant to or has a contraindication to these treatments.)

^{IX} Off-licence

	<p>biologic agent seek advice from a clinician with expertise in biologic therapy and consider any of the following strategies:</p> <ul style="list-style-type: none"> reiterate advice about modifiable factors contributing to poor response (for example, obesity and poor adherence) optimise adjunctive therapy (for example, switch from oral to sub-cutaneous methotrexate) switch to an alternative biologic agent consider non-biologic therapy approaches (for example inpatient topical therapy or standard systemic therapy) 	
Transitioning to/between biologic therapies		
R25	<p>When choosing the transitioning strategy from one drug therapy to another and whether a therapy washout (or no washout) should be used, take into consideration:</p> <ul style="list-style-type: none"> the pharmacology of the drugs that are being started and stopped (see Toolkit A: Summary of licensed indications and posology for biologic therapy, in <i>Supporting information 2</i>) the person's clinical circumstances the person's views on the risks and benefits of transitioning option(s) 	↑↑
R26	<p>Consider the following strategies when transitioning from standard systemic to biologic therapy:</p> <ul style="list-style-type: none"> in stable disease, aim to allow 1 month to elapse between the last dose of any current standard systemic immunosuppressant psoriasis therapy (except methotrexate) and the planned date of biologic initiation start a biologic therapy with no drug washout period in people taking methotrexate, or in people on other therapies where this would lead to unstable disease when standard, systemic immunosuppressant therapy cannot be stopped (for example, in people for whom a disease flare would be severe or hazardous), rationalise use of therapy and stop as soon as possible (for example, when a minimum response has been achieved) 	↑
R27	<p>When transitioning to a new biologic therapy (from a previous biologic therapy) consider using a 1-month washout period, or the length of the treatment cycle (whichever is longer), between the last dose of the current biologic therapy and the planned date of biologic initiation</p>	↑
Conception and pregnancy		
R28	<p>Provide information about the possible effects of biologic therapy during conception and pregnancy including:</p> <ul style="list-style-type: none"> the importance of controlling severe or unstable psoriasis to maintain maternal health that most pregnancies reported in women taking biologic therapy at conception and during pregnancy have successful outcomes that evidence about the effect of biologic therapy on conception and pregnancy mostly relates to TNF antagonists in women with rheumatological and inflammatory bowel disease; this evidence indicates a potential risk associated^x 	↑↑

^x Major congenital malformations reported in 3.6-5.0% of women exposed to anti-TNF compared with 1.5-4.7% in control groups (odds ratios [OR] = 1.32-1.64)

	<p>with exposure to TNF antagonists but is of low quality, and may relate to other factors (for example, other co-therapies or the underlying disease)</p> <p>that the risk of fetal abnormalities in women with psoriasis who conceive on biologic therapy has not been adequately studied and therefore cannot be quantified</p> <ul style="list-style-type: none"> • that maternal IgG, and therefore biologic drugs currently licensed for psoriasis, are actively transferred to the developing fetus during the second and third trimester and that the impact of this on fetal and neonatal development and risk of infection has not been adequately studied • that live vaccines must be avoided in infants born to mothers taking biologic therapy beyond 16 weeks' gestation • relevant patient information resources^{XI} 	
R29	Advise women of child-bearing potential who are starting biologic therapy for psoriasis to use effective contraception ^{XII} and discuss conception plans with the consultant supervising their care (see R30)	↑↑
R30	<p>Discuss the risks and benefits of continuing versus stopping biologic therapy with women who are of child-bearing potential or who become pregnant. Offer advice on a case-by-case basis by taking into account the woman's views and the:</p> <ul style="list-style-type: none"> • course of psoriasis disease and the fetal outcome during any prior pregnancies • risk of severe or unstable psoriasis if the biologic therapy were stopped • physical, psychological and social functioning if the biologic therapy were stopped • options for alternative, non-biologic treatment strategies 	↑↑
R31	Assess whether biologic therapy for psoriasis can be stopped in women who become pregnant. Ensure consultation and information-sharing across specialities including with an obstetrician who has expertise in caring for pregnant women with medical problems. Collect pregnancy outcome data for safety registries, for example BADBIR in the U.K. and Republic of Ireland.	↑↑
R32	Advise mothers who have received biologic therapy for psoriasis beyond 16 weeks' gestation that their infants should not receive any live vaccinations until they have reached 6 months of age (for example, rotavirus and BCG)	↑↑
Biologic therapy and cancer risk		
R33	<p>Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to:</p> <ul style="list-style-type: none"> • their past or current history of cancer (see R35) and/or • any future risk of cancer 	↑↑
R34	Provide information to people with psoriasis about the importance of participating in national cancer screening programmes	↑↑
R35	<p>Exercise caution and discuss with the relevant cancer specialist when prescribing biologics in people with psoriasis and:</p> <ul style="list-style-type: none"> • a history of cancer, particularly if this has been diagnosed and treated <5 years previously and/or • where the baseline risk of skin cancer is increased (for example, previously treated non-melanoma skin cancer (NMSC)) 	↑↑

^{XI} For example, <http://www.medicinesinpregnancy.org/Medicine--pregnancy>

^{XII} There are no known interactions between biologic therapies and contraceptive methods (see drug-specific SPCs)

Biologic therapy and infections		
R36	Assess people with psoriasis prior to, and during treatment with, biologic therapy with respect to: <ul style="list-style-type: none"> • risk factors for infection (for example, co-morbidities, co-therapy, lifestyle and travel) • known infections (past or current) • signs or symptoms suggestive of infection 	↑↑
Biologic therapy and chronic viral infections – hepatitis B, hepatitis C and HIV		
R37	Test for hepatitis B (surface antigen and core antibody), hepatitis C (IgG) and HIV (HIV-1 and HIV-2 antibody and HIV-1 antigen) infection in people starting biologic therapy	↑↑
R38	Consider ongoing screening (for example annually) for hepatitis B, hepatitis C and HIV, particularly in people who belong to a group at increased risk of infection ^{xiii} (see Toolkit B: Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV, in <i>Supporting information 2</i>)	↑
R39	Retest for viral hepatitis in any person who develops unexplained transaminitis (raised ALT and/or AST); retest for HIV infection in any person who has symptoms of HIV seroconversion.	↑↑
R40	Consult a hepatitis specialist when treating all people with biologic therapy who have hepatitis B or C infection, whether newly-diagnosed or previously known	↑↑
R41	Provide treatment options to people with psoriasis who are HIV seropositive on a case-by-case basis; be aware that severe psoriasis can occur in people with uncontrolled HIV infection. Involve relevant specialists and ensure HIV viral load is suppressed on ART before considering biologic therapy.	↑↑
R42	Test for varicella zoster (VZ) virus antibody in people with a negative or uncertain history for chickenpox; consider varicella vaccination in those who are not varicella-immune and seek expert advice. Be aware of the indications for using VZ immunoglobulin in VZ-susceptible individuals. ^{xiv}	GPP (Good Practice Point)
Use of biologic therapy and TB		
R43	Screen for latent TB with an interferon-gamma release assay. Arrange a plain chest radiograph to rule out abnormalities at baseline including granulomas indicative of prior infection and other confounding lung diseases. If positive, assess for active TB and/or management of latent TB in consultation with a TB specialist (see Tuberculosis NICE guideline ^{xv})	↑↑
R44	In people who require treatment for latent TB (3 months of isoniazid (with pyridoxine) and rifampicin, or 6 months of isoniazid (with pyridoxine)) aim to complete 2 months' treatment before commencing biologic therapy	↑↑
R45	Any symptoms or signs suggestive of TB, or new exposure to TB or prolonged residence in a high-incidence setting should prompt further clinical assessment and investigation, including a repeat interferon-gamma release assay. Be aware that active TB on TNF	↑↑

^{xiii} HIV testing and prevention: People who should be offered an HIV test (NICE and BHIVA guidelines); Offering and providing hepatitis B and C tests (NICE guidance) and BHIVA guidelines for routine investigation and monitoring of adult HIV-1-infected individuals www.bhiva.org/documents/Guidelines/Monitoring/160606-Monitoring-gl-draft-for-Consultation.pdf

^{xiv} https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/559469/VZIG_ChickenPox_v4.pdf

^{xv} NICE guidelines. Tuberculosis NG33 <https://www.nice.org.uk/guidance/ng33>

	antagonist therapy is often disseminated and extrapulmonary; symptoms may include unexplained weight loss, night sweats, non-resolving cough, haemoptysis and lymphadenopathy.	
R46	Inform people that they should seek medical advice if symptoms of tuberculosis develop during or after treatment with a biologic therapy and issue a patient alert card in line with MHRA guidance) ^{xvi}	↑↑
Biologics and vaccination		
R47	Do not give live vaccines to people on biologic therapy or to infants (up to 6 months of age) whose mothers have received biologic therapy beyond 16 weeks' gestation	↓↓
R48	Stop biologic therapy for at least 6 months before giving live vaccines, and for 12 months in the case of Shingles (herpes zoster) vaccine. In general, biologic therapy can be started 4 weeks after administration of a live vaccine. Refer to the drug-specific SPC and Green Book (Immunisation against infectious disease) ^{xvii} for further information.	↑↑
R49	Provide people on biologic therapy information on safe use of vaccinations including which vaccination should be used and which to avoid (see BAD Patient Information Leaflet on immunisation ^{xviii} and the Green Book, ^{xvii} with reference to the clinical risk category 'immunosuppression')	↑↑
R50	Where possible, complete all required vaccinations prior to initiation of biologic therapy and review vaccination requirements during therapy with reference to the Green Book ^{xvii} and the clinical risk category 'immunosuppression'	↑↑
Important contraindications to biologic therapies (Good Practice Point, GPP)		
R51	Do not use TNF antagonists in people with demyelinating diseases and review alternative interventions in people who have an affected first-degree relative with demyelinating disease	GPP
R52	Stop treatment and seek specialist advice if neurological symptoms suggestive of demyelinating disease ^{xix} develop during TNF antagonist therapy	GPP
R53	Avoid TNF antagonist therapy in people with severe (NYHA class III and IV) cardiac failure	GPP
R54	Assess people with well-compensated (NYHA class I and II) cardiac failure ^{xx} and consult with a cardiology specialist before using TNF antagonist therapy	GPP
R55	Stop TNF antagonist therapy in the event of new or worsening pre-existing heart failure and seek specialist advice	GPP
R56	Exercise caution and consult a gastroenterology specialist before using secukinumab or ixekizumab in people with inflammatory bowel disease	GPP
R57	In people undergoing elective surgery balance the potential benefit of preventing post-operative infection by stopping biologic therapy against the risk of developing severe or unstable disease. Advise stopping biologic therapy 3 to 5 times the half-life of the drug in	GPP

^{xvi} <https://www.gov.uk/drug-safety-update/tumour-necrosis-factor-alpha-inhibitors>

^{xvii} www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book

^{xviii} www.bad.org.uk/leaflets

^{xix} Loss or reduction of vision in one eye with painful eye movements; double vision; ascending sensory disturbance and/or weakness; problems with balance, unsteadiness or clumsiness; altered sensation travelling down the back and sometimes into the limbs when bending the neck forwards (Lhermitte's symptom); please see NICE guidelines CG186 www.nice.org.uk/guidance/cg186

^{xx} Please see NICE Pathway <https://pathways.nice.org.uk/pathways/chronic-heart-failure#path=view%3A/pathways/chronic-heart-failure/diagnosing-and-assessing-chronic-heart-failure.xml&content=view-node%3Anodes-history-examination-and-referral>

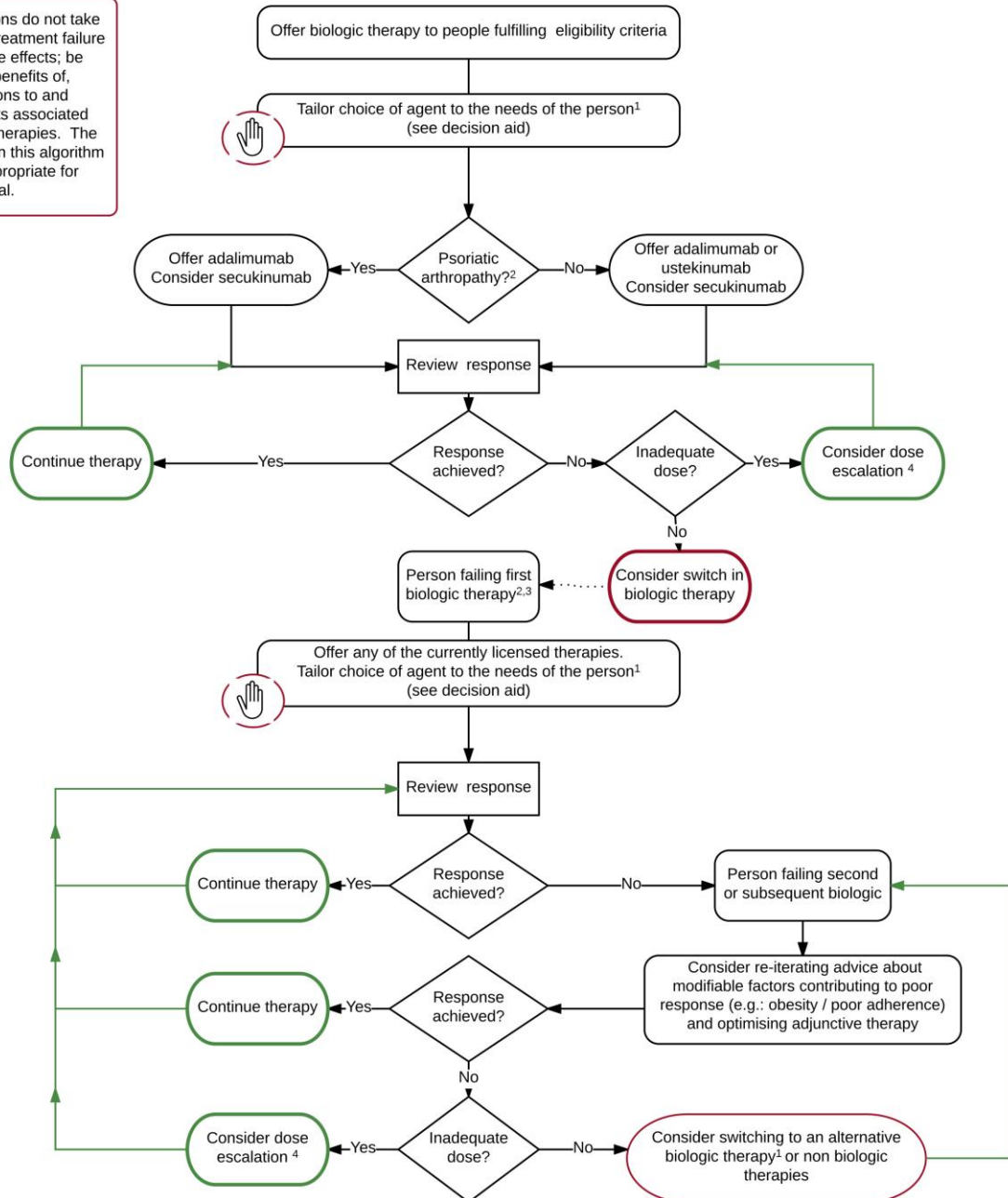
question (see Toolkit A: Summary of licensed indications and posology for biologic therapy, in *Supporting information 2*) or the length of the treatment cycle (whichever is longer) between the last dose of therapy and the planned surgery. Inform the surgical team that the patient may be at a higher risk of infection post-operatively. Restart biologic therapy postoperatively if there is no evidence of infection and wound healing is satisfactory.

Table 2. List of key recommendations

ALGORITHM

Pathway algorithm to guide Choice of Biologic therapy in Adults with Psoriasis
Please use in conjunction with the summary of recommendations

Pathway options do not take into account treatment failure due to adverse effects; be aware of the benefits of, contraindications to and adverse effects associated with biologic therapies. The choice given in this algorithm will not be appropriate for every individual.



NOTES

1. Take into account psoriasis factors (the goal of therapy e.g. PGA clear/nearly clear; disease phenotype and pattern of activity; disease severity and impact; presence of psoriatic arthritis; outcomes of previous treatment for psoriasis) and other factors (age; past or current co-morbid conditions; conception plans; body weight).
2. Take into account both psoriasis and psoriatic arthritis before initiating or making changes to biologic therapy, and manage treatment in consultation with a rheumatologist; be aware that the presence of and phenotype of psoriatic arthritis (for example, peripheral versus axial disease) may influence access to, choice and dose of, biologic therapy.
3. Consider changing to an alternative biologic therapy if any of the following applies: the psoriasis does not achieve the minimum response criteria (primary failure – see R11) or the psoriasis initially responds but subsequently loses this response (secondary failure)
4. Consider escalating the dose of biologic therapy in adults (R22) when an inadequate primary response may be due to insufficient drug dosing (for example, in people who are obese or whose psoriasis relapses during the treatment cycle). Take into account that dose escalation may be associated with an increased risk of infection, and, depending on the drug, off-licence and not funded. Currently, a dose-escalation strategy is not applicable to secukinumab or ixekizumab.
5. This guidance applies to biosimilars, subject to recommendations given within the BAD position statement and EMA guidelines.^{4,5}

DECISION AID

This table supports the decision-making process during the consultation for patients and clinicians before the initiation of biologic therapy. It is complementary to the existing patient information leaflets (PILs; www.bad.org.uk/leaflets). All biologic therapies for the treatment of psoriasis require bloods tests before and during treatment. If you have psoriatic arthritis, your doctor will take this into consideration.

Frequently Asked Questions	Adalimumab	Etanercept	Infliximab	Ixekizumab	Secukinumab	Ustekinumab	No active treatment
How often do I need to inject the treatment?	1 injection under the skin Every other week	1 injection under the skin Once or twice a week	1 injection in the vein Every 8 weeks	1 injection under the skin Every 2 weeks for the first 3 months, every 4 weeks thereafter	2 injections under the skin Every 4 weeks	1 injection under the skin Every 12 weeks	Does not apply
Who gives the treatment?	You or your carer will learn to give the injection after training.	You or your carer will learn to give the injection after training.	You will need to go to hospital where the injection will be given by a healthcare professional.	You or your carer will learn to give the injection after training	You or your carer will learn to give the injection after training.	You may choose to have the injection given to you by a nurse in your home. Alternatively, you or your carer may learn to give the injection after training.	Does not apply
How long has this treatment been around for?	Since 2008	Since 2004	Since 2006	Anticipated to be available in 2017	Since 2015	Since 2009	Does not apply
How many people become clear or nearly clear of psoriasis because of this treatment?^{xxi}	Around 341 per 1000 people after 3-4 months of treatment ⁶	Around 227 per 1000 people after 3-4 months of treatment ⁶	Around 451 per 1000 people after 3-4 months of treatment ⁶	Around 682 per 1000 people after 3-4 months of treatment ⁶	Around 579 per 1000 people after 3-4 months of treatment ⁶	Around 413 per 1000 people after 3-4 months of treatment ⁶	Roughly 20 per 1000 people become clear or nearly clear with placebo (sham injection) after 3-4 months ⁶

^{xxi} The evidence is drawn from clinical trials including a mixed biologic-naïve and experienced population

In U.K. clinical practice, what are the chances of staying on this treatment past 1 year? ^{xxii}	77-81% chance ⁷	67-73% chance ⁷	54-74% chance ⁷	Not known at present	Not known at present	86-92% chance ⁷	Does not apply
How many people experience unwanted effects that are serious enough to stop the treatment? ^{xxi, xxiii}	Up to 2 per 1000 people after 3-4 months of treatment ⁶	Up to 10 per 1000 people after 3-4 months of treatment ⁶	Up to 82 per 1000 people after 3-4 months of treatment ⁶	Up to 39 per 1000 people after 3-4 months of treatment ⁶	Up to 5 per 1000 people after 3-4 months of treatment ⁶	Up to 1 per 1000 people after 3-4 months of treatment ⁶	Roughly 19 per 1000 people taking a placebo (sham injection) withdraw after 3-4 months of monitoring ⁶
How many people experience an infection serious enough to lead to admission into hospital because of this treatment? ^{xxiii}	Up to 11 per 1000 people after 3-4 months of treatment ⁸	Up to 6 per 1000 people after 3-4 months of treatment ⁸	Up to 41 per 1000 people after 5-7 months of treatment	Up to 11 per 1000 people after 3-4 months of treatment	Up to 10 per 1000 people after 3-4 months of treatment ⁸	Up to 4 per 1000 people after 3-4 months of treatment ⁸	Roughly 4 per 1000 people taking a placebo (sham injection) after 3-4 months of monitoring ⁸
What conditions would make your doctor hesitant about giving you the treatment?	Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis)	Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis)	Moderate or severe heart failure, demyelinating disorders (e.g. multiple sclerosis)	Inflammatory bowel disease (i.e. Crohn's disease or ulcerative colitis), recurrent candida infection (i.e. thrush)	Inflammatory bowel disease (i.e. Crohn's disease or ulcerative colitis), recurrent candida infection (i.e. thrush)	No particular condition	Does not apply

^{xxii} The evidence is drawn from a real-world UK biologic-naïve population; it may not apply to biologic choice for subsequent lines of treatment

^{xxiii} The figures are drawn from the upper limit of the 95% confidence interval from a meta-analysis of clinical trials and reflect the risk that has been excluded; differences amongst biologic therapies should be interpreted with caution

What if I want to have children?	Women and men have had children on this treatment. The risk to the baby is unknown. Your dermatologist will discuss this with you.	Women and men have had children on this treatment. The risk to the baby is unknown. Your dermatologist will discuss this with you.	Women and men have had children on this treatment. The risk to the baby is unknown. Your dermatologist will discuss this with you.	The risk to the baby is unknown. Your dermatologist will discuss this with you.	The risk to the baby is unknown. Your dermatologist will discuss this with you.	The risk to the baby is unknown. Your dermatologist will discuss this with you.	During pregnancy, psoriasis may get better, stay the same, or become worse
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Table 3. Decision aid. NICE eligibility criteria, infliximab: PASI ≥ 20 , DLQI >18 ; other biologic therapies: PASI ≥ 10 , DLQI >10

SUGGESTED SCHEDULE FOR SCREENING AND MONITORING

		Baseline ^{xxiv}	Monitoring ^{xxiv}
History/symptom enquiry			
Psoriasis	Disease phenotype; course (stable/unstable); response & adverse effects to prior therapies	Yes	Ongoing
Psoriatic arthritis	Screen for psoriatic arthritis (e.g. using the PEST questionnaire ^{xxv}); for people with psoriatic arthritis symptom enquiry to assess control	Yes	Every 12 months
Identification of contraindications to therapy and/or development of therapy-induced toxicity	Thorough history, symptom enquiry	Yes	Every 3-6 months
Infection	Any past or current chronic infection including tuberculosis, candidiasis	Yes	Every 3-6 months
	Identify risk factors for tuberculosis, hepatitis B, C and HIV ^{xxvi}		
	Ascertain history for chickenpox		N/A
Alert card ^{xxvii}	Ensure people carry an alert card with them at all times in line with MHRA guidance	Yes	At each review appointment
Cardiovascular assessment ^{xxviii}	Include symptom enquiry about heart failure [NYHA III. Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation or dyspnea. NYHA IV. Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.]	Yes	Clinical assessment every 3-6 months

^{xxiv} Additional assessment and monitoring may be required in patients on concomitant therapy or in certain clinical circumstances

^{xxv} www.bad.org.uk/healthcare-professionals/forms-downloads

^{xxvi} See Toolkit B: Groups at increased risk of tuberculosis, hepatitis B, hepatitis C and HIV, in *Supporting information 2*

^{xxvii} <https://www.gov.uk/drug-safety-update/tumour-necrosis-factor-alpha-inhibitors>

^{xxviii} Evidence of demyelination/heart failure may preclude use of TNF antagonists

Neurological assessment ^{xxviii}	Past or current history or symptoms of demyelinating disease ^{xxviii}	Yes	Every 3-6 months
Gastrointestinal assessment ^{xxix}	Past of current history or symptoms of inflammatory bowel disease	Yes	Every 3-6 months
Malignancy	Any past or current malignancy (including skin cancer)	Yes	Every 3-6 months
	Ensure concordant with national cancer screening programmes		
	Gynaecological review of patients with history of cervical dysplasia		
BADBIR	Offer the opportunity to participate	Yes	Every 6 months (to complete follow-up data)
Clinical assessments			
Psoriasis disease severity assessment	Goal of therapy, e.g. a PGA of clear or nearly clear	Yes	To establish disease response; every 6 months thereafter
	PASI (or BSA if PASI not applicable)		
	DLQI		
Skin cancer	Full skin examination	Yes	As indicated by risk at baseline and in the context of immunosuppression
Psoriatic arthritis	Consult with a rheumatologist	Yes	To establish disease response; every 3-6 months thereafter and/or as clinically indicated
General physical examination	To identify contra-indications to therapy and/or development of therapy-induced toxicity	Yes	As indicated by history/symptom enquiry
Investigations			
Blood tests	Full blood count; creatinine and electrolytes; liver function tests	Yes	At 3-4 months; every 6 months thereafter and/or as clinically indicated
	Hepatitis B (surface antigen and core antibody) hepatitis C (IgG)		If clinically indicated, e.g. transaminitis (raised ALT and/or AST), or ongoing (annually) in people who belong to a

^{xxix} Exercise caution using secukinumab in people with inflammatory bowel disease

			group at increased risk of infection ^{xxvi}
	Human immunodeficiency virus (HIV-1 and HIV-2 antibody, and HIV-1 antigen)		If clinically indicated, e.g. symptoms of seroconversion, or ongoing (annually) in people who belong to a group at increased risk of infection ^{xxvi}
	Autoantibodies (anti-nuclear antibodies, anti-nuclear double-stranded DNA antibodies)		If symptoms or signs suggest development of autoimmune phenomena, e.g. transaminitis (raised ALT and/or AST)
	Test for varicella zoster virus antibody in people with a negative or uncertain history for chickenpox		Consider varicella vaccination in those who are not varicella-immune and seek expert advice; be aware of the indications for using VZ immunoglobulin in VZ-susceptible individuals ^{xxx}
Tuberculosis	Interferon-gamma release assay and chest X-ray	Yes	If clinically indicated, e.g. symptoms or signs of tuberculosis, new exposure to tuberculosis or residence in high-incidence setting
Urine	Urine analysis	Yes	If clinically indicated
	Urine pregnancy test		

Table 4. Suggested schedule for screening and monitoring

^{xxx} https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/559469/VZIG_ChickenPox_v4.pdf

AUDIT STANDARDS, DATA ITEMS AND DATA COLLECTION METHODOLOGY

Dermatology teams involved in prescribing biologic interventions should use audit as a tool to monitor their service against national guidelines of care. The aim should be to ensure that the service is high in quality, safe and cost-effective. See Toolkit C: Audit standards, data items and data collection methodology, in *Supporting information 2*, for further details.

STAKEHOLDER INVOLVEMENT AND PEER REVIEW

The full version of the guideline was made available to the BAD membership, British Society for Paediatric Dermatology, British Dermatological Nursing Group, Primary Care Dermatological Society, British Society for Paediatric and Adolescent Rheumatology, British Society of Rheumatology, Royal College of Obstetrics and Gynaecology, Psoriasis and Psoriatic Arthritis Alliance, Psoriasis Association and relevant pharmaceutical companies (see Appendix F, in *Supporting information 1*, for the full list of stakeholders), comments from whom were actively considered by the GDG. Following further review, the finalized version was peer-reviewed by the Clinical Standards Unit of the BAD, made up of the Therapy & Guidelines Sub-committee (T&G), prior to submission for publication.

LIMITATIONS OF THE GUIDELINE

This document has been prepared on behalf of the BAD and is based on the best data available when the document was prepared. It is recognized that under certain conditions it may be necessary to deviate from the guidelines and that the results of future studies may require some of the recommendations herein to be changed. Failure to adhere to these guidelines should not necessarily be considered negligent, nor should adherence to these recommendations constitute a defence against a claim of negligence. Limiting the review to English language references was a pragmatic decision but the authors recognize this may exclude some important information published in other languages.

PLANS FOR GUIDELINE REVISION

This 2017 guideline updates the previous version.⁹ An annual literature review is planned for this fast-moving subject and the recommendations updated where necessary, in line with the BAD's recommended guideline development methodology.¹

SUPPORTING INFORMATION

The full version of this guideline is available in the online *Supporting information 1* document, which includes tables linking evidence to recommendations (LETR), details of the network meta-analysis, summary of included studies, forest plots, GRADE evidence profiles, PRISMA flow diagrams, list of excluded studies and search strategies. *Supporting information 2* contains toolkits to aid implementation.

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FOOTNOTE

This is an updated guideline prepared for the BAD Clinical Standards Unit, which includes the Therapy & Guidelines sub-committee. Members of the Clinical Standards Unit that have been involved are: PM McHenry [Chairman T&G], K Gibbon [BAD Assistant Honorary Secretary], DA Buckley, TA Leslie, EC Mallon, S Wakelin, S Ungureanu, RYP Hunasehally, M Cork, GA Johnston, J Natkunarajah, FS Worsnop, N Chiang, G Petrof, J Donnelly [British National Formulary], C Saunders [British Dermatological Nursing Group], AG Brain [BAD Scientific Administrator], LS Exton [BAD Information Scientist], MF Mohd Mustapa [BAD Clinical Standards Manager].

CONFLICTS OF INTEREST

Details of declarations of interests (cumulative, throughout the project) can be found in the full version of the guideline (Appendix A, in *Supporting information 1*) and are consistent with NICE Accreditation policy.

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